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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/535,235

12/19/2005

Alex Cimpola

SHIRE-518

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03/31/2008

MILLEN, WHITE, ZELANO & BRANIGAN, P.C.

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ARLINGTON, VA 22201

EXAMINER

ARIANI, KADE

ART UNIT

PAPER NUMBER

1651

MAIL DATE

DELIVERY MODE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/535,235	<b>Applicant(s)</b> CIMPOIA ET AL.	
	<b>Examiner</b> KADE ARIANI	<b>Art Unit</b> 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-24 is/are rejected.
- 7) ☒ Claim(s) 1 and 12 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. ____.                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>7/15/2005</u> .   | 6) <input type="checkbox"/> Other: ____.                          |

## ***DETAILED ACTION***

Claims 1-24 are pending in this application and were examined on their merits.

### ***Claim Objection***

Claims 1 and 12 is objected to because of the following informalities:

The recitation –subjecting a compounds-- in claims 1 and 12 is incorrect.

Appropriate correction is required.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cimpoia et al. (WO 00/47759) in view of Janes et al. (in IDS, J. Org. Chem., 1999, Vol. 64, p.9019-9029) and further in view of Ferrero et al. (Monatshefte für Chemie, 2000, Vol. 131, p.585-616).

Claims 1-11 are drawn to a process comprising the steps of a) subjecting a compound of formula II to an enzymatic resolution in the presence of pig liver esterase or porcine pancreatic lipase, b) recovering compound of formula I, wherein R<sub>1</sub> is C<sub>1-12</sub>

alkyl, and  $R_2$  is  $\text{CO-C}_{6-12}$  aryl, wherein  $R_1$  is methyl and  $R_2$  is benzoyl, the process further comprising a) replacing the functional group at position C4 of the compound of formula I to produce a compound of formula V, b) removing the  $R_2$  group, c) recovering a compound of formula VI, wherein B is purine (or pyrimidine) base, wherein  $R_3, R_4, R_5, R_6, R_7$ , and  $R_8$  are H, and further recovering a compound of formula VII.

Claims 12-24 are drawn to a process for producing a compound of formula III comprising the steps of a) subjecting a compound of formula IV to an enzymatic resolution in the presence of lipase, b) recovering compound of formula III, wherein  $R_{11}$  is  $\text{C}_{1-12}$  alkyl and  $R_{12}$  is a hydroxyl protecting group  $\text{CO-C}_{6-12}$  aryl, wherein  $R_{11}$  is methyl and  $R_{12}$  is benzoyl, wherein the enzyme is *Candida Antarctica* lipase A, *C. Antarctica* lipase B, *C. Lypolitica* lipase, *R. Miehei* lipase, the process further comprising a) replacing the functional group at position C4 of the compound of formula III to produce a compound of formula VIII, b) removing the  $R_{12}$  group, c) recovering a compound of formula IX, wherein B is purine (or pyrimidine) base, wherein  $R_3, R_4, R_5, R_6, R_7$ , and  $R_8$  are H, and further recovering a compound of formula X.

Cimpoia et al. teach a process comprising the steps of a) subjecting a dioxolane compound (formula II, formula IV) to an enzymatic resolution in the presence of horse liver esterase and various lipases, b) recovering the resulted compound, wherein  $R_1$  is  $\text{C}_{1-12}$  alkyl, and  $R_2$  is  $\text{CO-C}_{6-12}$  aryl, wherein  $R_1$  is methyl and  $R_2$  is benzoyl (wherein  $R_{11}$  is  $\text{C}_{1-12}$  alkyl and  $R_{12}$  is a hydroxyl protecting group  $\text{CO-C}_{6-12}$  aryl, wherein  $R_{11}$  is methyl and  $R_{12}$  is benzoyl), the process further comprising a) replacing the functional group at position C4 of the compound, removing the  $R_2$  group ( $R_{12}$  group), recovering a compound of (formula VI, formula IX) wherein B is purine (or pyrimidine) base, wherein

R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub>, and R<sub>8</sub> are H, and further recovering the compound of (formula VII , formula X) (see Abstract, page 4, page 7 2<sup>nd</sup>-4<sup>th</sup> paragraphs, page 8 2<sup>nd</sup> paragraph, page 11 2<sup>nd</sup> and 3<sup>rd</sup> paragraphs).

Cimpoia et al. further teach modifications and variations of the present invention including but not limited to selection of enzymes and optimization of reaction conditions will be obvious (page 68 end paragraph).

Cimpoia et al. do not teach pig liver esterase, porcine pancreatic lipase, *Candida Antarctica* lipase A, *C. Antarctica* lipase B, *C. Lypolitica* lipase, and *R. Miehei* lipase. However, Janes et al. teach *Antarctica* lipase A, *C. Lypolitica* lipase, *R. Miehei* lipase (p.9022, Table 1.) Furthermore Ferrero et al. teach *Antarctica* lipase B is one of the enzymes commonly uses in biocatalytic processes (p.586 Table 1.).

Janes et al. further teach dioxolane nucleosides are powerful antiviral and anticancer drugs. Janes et al. further teach the commercial availability, relatively low cost, and tolerance for a wide class of substrates make hydrolytic enzymes attractive biocatalysts (Abstract, and p.9020 2<sup>nd</sup> column 2<sup>nd</sup> paragraph).

Therefore, it would have been obvious to one of ordinary skill in the art to modify the process as taught by Cimpoia et al. by substituting the enzymes with the esterase and lipases as taught by Janes et al. and Ferrero et al. to provide a process for producing dioxolane nucleoside analogues. The claims would have been obvious because substitution of one known element (lipase) for another would have yielded the predictable results to one of ordinary skill in the art at the time the invention was made.

### **Conclusion**

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kade Ariani whose telephone number is (571) 272-6083. The examiner can normally be reached on 9:00 am to 5:30 pm EST Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford Jr/  
Primary Examiner, Art Unit 1651

Kade Ariani  
Examiner  
Art Unit 1651